Organophosphate Flame Retardants, Highly Fluorinated Chemicals, and Biomarkers of Placental Development and Disease During Mid-Gestation.

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Public Summary:
Perfluoroalkyl and polyfluoroalkyl substances (PFASs) and organophosphate flame retardants (OPFRs) are chemicals that may contribute to placenta-mediated complications and adverse maternal-fetal health risks. Few studies have investigated these chemicals in relation to biomarkers of effect during pregnancy. We measured 12 PFASs and four urinary OPFR metabolites in 132 healthy pregnant women during mid-gestation and examined a subset with biomarkers of placental development and disease (n = 62). Molecular biomarkers included integrin alpha-1 (ITGA1), vascular endothelial-cadherin (CDH5), and matrix metalloproteinase-1 (MMP1). Morphological endpoints included potential indicators of placental stress and the extent of cytotrophoblast (CTB)-mediated uterine artery remodeling. Serum PFASs and urinary OPFR metabolites were detected in approximately 50%-100% of samples. The most prevalent PFASs were perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), and perfluorooctane sulfonic acid (PFOS), with geometric mean (GM) levels of approximately 1.3-2.8 (95% confidence limits from 1.2-3.1) ng/ml compared to </=0.5 ng/ml for other PFASs. Diphenyl phosphate (DPhP) and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) were the most prevalent OPFR metabolites, with GMs of 2.9 (95% CI: 2.5-3.4) and 3.6 (95% CI: 2.2-3.1) ng/ml, respectively, compared to <1 ng/ml for bis(2-chloroethyl) phosphate (BCEP) and bis(1-chloro-2-propyl) phosphate (BCIPP). We found inverse associations of PFASs or OPFRs with ITGA1 or CDH5 immunoreactivity and positive associations with indicators of placental stress in multiple basal plate regions, indicating these chemicals may contribute to abnormal placentation and future health risks. Associations with blood pressure and lipid concentrations warrant further examination. This is the first study of these chemicals with placental biomarkers measured directly in human tissues and suggests specific biomarkers are sensitive indicators of exposure during a vulnerable developmental period.

Scientific Abstract:
Perfluoroalkyl and polyfluoroalkyl substances (PFASs) and organophosphate flame retardants (OPFRs) are chemicals that may contribute to placenta-mediated complications and adverse maternal-fetal health risks. Few studies have investigated these chemicals in relation to biomarkers of effect during pregnancy. We measured 12 PFASs and four urinary OPFR metabolites in 132 healthy pregnant women during mid-gestation and examined a subset with biomarkers of placental development and disease (n = 62). Molecular biomarkers included integrin alpha-1 (ITGA1), vascular endothelial-cadherin (CDH5), and matrix metalloproteinase-1 (MMP1). Morphological endpoints included potential indicators of placental stress and the extent of cytotrophoblast (CTB)-mediated uterine artery remodeling. Serum PFASs and urinary OPFR metabolites were detected in approximately 50%-100% of samples. The most prevalent PFASs were perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), and perfluorooctane sulfonic acid (PFOS), with geometric mean (GM) levels of approximately 1.3-2.8 (95% confidence limits from 1.2-3.1) ng/ml compared to </=0.5 ng/ml for other PFASs. Diphenyl phosphate (DPhP) and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) were the most prevalent OPFR metabolites, with GMs of 2.9 (95% CI: 2.5-3.4) and 3.6 (95% CI: 2.2-3.1) ng/ml, respectively, compared to <1 ng/ml for bis(2-chloroethyl) phosphate (BCEP) and bis(1-chloro-2-propyl) phosphate (BCIPP). We found inverse associations of PFASs or OPFRs with ITGA1 or CDH5 immunoreactivity and positive associations with indicators of placental stress in multiple basal plate regions, indicating these chemicals may contribute to abnormal placentation and future health risks. Associations with blood pressure and lipid concentrations warrant further examination. This is the first study of these chemicals with placental biomarkers measured directly in human tissues and suggests specific biomarkers are sensitive indicators of exposure during a vulnerable developmental period.

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